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Filing Date	October 26, 2000		
First Named Inventor	Chapman		
Group Art Unit	1615		
Examiner Name	Kailash C. Srivastava		
Attorney Docket Number	18989-006 (BWH-6)		

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Exam Initials	Cite No.	U.S. Patent Document No.	Issue Date	Name of Patentee(s) or Applicant(s)	Class	Sub Class	Filing Date If Appropriate
	A1	5,157,019	10/20/92	Glover et al.			
	A2	5,164,295	11/17/92	Kisilevsky et al.			750
	A3	5,270,165	12/14/93	Van Nostrand et al.			1,0%
	A4	5,432,264	7/11/95	Grubb et al.		TEC	APR
	A5	5,866,318	2/2/99	Rydel et al.		10/7	CENT
	A6	6,033,893	3/7/00	Bandman et al.			159 1600

3 1.				FOREIGN PATENT DOCUMENTS			
Exam Initials	Cite No.	Foreig Office	n Patent Document Number	Name of Patentee(s) or Applicant(s)	Date of Publication	Tran Yes	slation No
	В1	-WO	94/01139	Baylor College of Medicine	- 1/20/94		-

*6		OTHER NON PATENT LITERATURE DOCUMENTS
Exam Initials	Cite No.	Name of Author, Title (when appropriate), Publication, Volume, Page(s), Date, Etc.
	C1	Abrahamson et al., "The human cystatin C gene (CST3), mutated in hereditary cystatin C amyloid angiopathy, is located on chromosome 20" 82 Hum. Genet. 223-26 (1989)
	C2	Allaire et al., "Local overexpression of TIMP-1 prevents aortic aneurysm degeneration and rupture in a rat model" 102 J. Clin. Invest. 1413-20 (1998)
	C3	Barrett <i>et al.</i> , "The place of human γ-trace (cystatin C) amongst the cysteine proteinase inhibitors" 120 Biochem. Biophys. Res. Commun. 631-36 (1984)
	C4	Bossard et al., "Proteolytic activity of human osteoclast cathepsin K: expression, purification, activation and substrate identification" 271 J. Biol. Chem. 12517-524 (1996)
	C5	Bromme et al., "Human cathepsin O2, a matrix protein-degrading cysteine protease expressed in osteoclasts: functional expression of human cathepsin in O2 in spodoptera frugiperda and characterization of the enzyme" 271 J. Biol. Chem. 2126-32 (1996)
	C6	Brown et al., "Chemical synthesis and cloning of a tyrosine tRNA gene" 68 Methods in Enzymology 109-151 (1979)
	C7	Buisson et al., "Up-regulation of a serine protease inhibitor in astrocytes mediates the neuroprotective activity of transforming growth factor β1" 12 FASEB J. 1683-91 (1998)
	C8	Calkins et al., 376 "Mammalian cysteine protease inhibitors: biochemical properties and possible roles in tumor progression" Biol. Chem. Hoppe Seyler 71-80 (1995)
	C9	Cao et al., "Transforming growth factor-β induces plasminogen activator inhibitor type-1 in cultured human orbital fibroblasts" 36 Invest. Orphthalmol. Vis. Sci. 1411-19 (1995)
	C10	Chapman et al., "Identification of cystatin C, a cysteine proteinase inhibitor, as a major secretory product of human alveolar macrophages in vitro" 141 Am. Rev. Respir. Dis. 698-705 (1990)
	C11	Chapman et al., "Comparison of live human neutrophil and alveolar macrophage elastolytic activity in vitro: relative resistance of macrophage elastolytic activity to serum and alveolar proteinase inhibitors"

Applicants: Chapman, et al. U.S.S.N.: 09/697,613



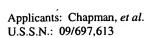
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	Lav	DELIGION PATENT LITERATURE DOCUMENTS
Exam Initials	Cite No.	Name of Author, Title (when appropriate), Publication, Volume, Page(s), Date, Etc. 74 J. Clin. Invest. 1693-700 (1984)
		74 J. Clin. Invest. 1693-700 (1984)
	C12	Chowdhury et al., "Long-term improvement of hypercholesterolemia after ex vivo gene therapy in LDLR-deficient rabbits" 254 Science 1802-805 (1991)
	C13	DeClerck et al., "Proteases and protease inhibitors in tumor progression" Adv. Exp. Med. Biol. 425:89-97 (1997)
	C14	Fabunmi <i>et al.</i> , "Expression of tissue inhibitor of metalloproteinases-3 in human atheroma and regulation in lesion-associated cells: a potential protective mechanism in plaque stability" 83 Cir. Res. 270-78 (1998)
	C15	Fruebis et. al., "A comparison of the antiatherogenic effects of probucol and of a structural analogue of probucol in low density lipoprotein receptor-deficient rabbits" 94 J. Clin. Invest. 392-98 (1994)
	C16	Gacko et al., "Distribution, activity and concentration of cathepsin B and cystatin C in the wall of aortic aneurysm" 50(2) Pol. J. Pathol. 83-86 (1999)
	C17	Galis et al., "Enhanced expression of a vascular matrix metalloproteinases induced in vitro by cytokines and in regions of human atherosclerotic lessions" 748 Ann. N.Y. Acad. Sci. 501-7 (1995)
· · · · · · · · · · · · · · · · · · ·	C18	Gelb et al., "Pycnodysostosis, a lysosomal disease caused by cathepsin K deficiency" 273 Science 1236-38 (1996)
	C19	Gething & Sambrook, "Cell-surface expression of influenza haemagglutinin from a cloned DNA copy of the RNA gene" 293 Nature 620-625 (1981)
	C20	Ghorpade et al., "Biochemistry and molecular regulation of matrix macromolecules in abdominal aortic aneurysms" 800 Ann. N.Y. Acad. Sci. 138-50 (1996)
	C21	Grainger <i>et al.</i> , "The serum concentration of active transforming growth factor-β is severely depressed in advanced atherosclerosis" 1 Nature Med. 74-79 (1995)
	C22	Hansson et al., "Detection of activated T lymphocytes in the human atherosclerotic plaque" 135 Am. J Path. 169-75 (1989)
	C23	Hirai et al., "Expression of cathepsin B and cystatin C in human colorectal cancer" 30(6) Hum. Pathol. 680-86 (1999)
	C24	Hiltke et al., "Structure/function analysis of human cystatin SN and comparison of the cysteine
		proteinase inhibitory profiles of human cystatins C and SN" 78(8) J. Dent. Res. 1401-409 (1999)
	C25	International Search Report, issued February 15, 2001
	C26	Ishibashi et al., "Massive xanthomatosis and atherosclerosis in cholesterol-fed low density lipoprotein receptor-negative mice" 93 J. Clin. Invest. 1885-893 (1994)
	C27	Ishiguro et al., "The use of monoclonal antibodies to define levels of cystatin C in normal human serum" 8 Hybridoma 303-13 (1989)
	C28	Johnatty <i>et al.</i> , Cytokine and chemokine regulation of proMMP-9 and TIMP-1 production by human peripheral blood lymphocytes" 158 J. Immunol. 2327-333 (1997)
	C29	Kafienah et al., "Human cathepsin K cleaves native type I and II collagens at the N-terminal end of the triple helix" 331 Biochem J. 727-32 (1998)
	C30	Knox et al., "Evidence for altered balance between Matrix metalloproteinases and their inhibitors in human aortic diseases" 95 Circulation 205-12 (1997)
•	C31	Kyse-Andersen <i>et al.</i> , "Serum cystatin C, determined by a rapid, automated particle-enhanced turbidimetric method, is a better marker than serum creatinine for glomerular filtration rate" 40 Clin. Chem. 1921-26 (1994)
	C32	Libby et al., "Macrophages and atherosclerotic plaque stability" 7 Curr. Opin. Lipidol. 330-35 (1996)
	C33	Littlewood-Evans et at., "The osteociast-associated protease cathepsin K is expressed in human breast carcinoma" 57 Cancer Res. 5386-390 (1997)
	C34	Mason et al., "Amino acid substitutions in the N-terminal segment of cystatin C create selective protein inhibitors of lysosomal cysteine proteinases" 330 (Pt. 2) Biochem J. 833-8 (1998)
	C35	Masucci et al., "A mouse model with features of familial combined hyperlipidemia" 275 Science 391-394 (1997)

Applicants: Chapman, et al.
U.S.S.N.: 09/697,613

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	iliya (OF OFFICE NON PATENT LITERATURE DOCUMENTS 1600/200
Exam Initials	Cite No.	Name of Author, Title (when appropriate), Publication, Volume, Page(s), Date, Etc.
	C36	McCaffrey <i>et al.</i> , "Genomic instability in the type II TGF-β1 Receptor gene in atherosclerotic and restenotic vascular cells" 100 J. Clin. Invest. 2182-88 (1997)
	C37	McMillan <i>et al.</i> , "In situ localization and quantification of mRNA for 92-kD type IV collagenase and its inhibitor in aneurysmal, occlusive, and normal aorta" 15 Arteriocler. Thromb. Vasc. Biol. 1139-44 (1995)
	C38	Merz et al., "Human cystatin C forms an inactive dimer during intracellular trafficking in transfected CHO Cells" 173 J. Cell Physiol. 423-32 (1997)
	C39	Merrifield et al., "Solid phase peptide synthesis. I. The synthesis of a tetrapeptide" 85 J. Am. Chem. Soc. 2149-2154 (1963)
	C40	Nycander et al., "Two-step mechanism of inhibition of cathepsin B by cystatin C due to displacement of the proteinase occluding loop" 422(1) FEBS Lett. 61-4
	C41	Olafsson, "The human cystatin C gene promoter: functional analysis and identification of heterogeneous mRNA" 55 Scand. J. Clin. Lab. Invest. 597-607 (1995)
	C42	Olsson et al., "The affinity and kinetics of inhibition of cysteine proteinases by intact recombinant bovine cystatin C" 1432(1) Biochim Biophys Acta 73-81 (1999)
	C43	Pearce et al., "Cellular components and features of immune response in abdominal aortic aneurysms" 800 Ann. N.Y. Acad. Sci. 175-85 (1996)
-	C44	Purcell-Huynh et al., "Transgenic mice expressing high levels of human apolipoprotein B develop severe atherosclerotic lesions in response to a high-fat diet" 95 J. Clin. Invest. 2246-257 (1995)
	C45	Randers et al., "Serum cystatin C as an endogenous marker of the renal function-a review" Clin. Chem. Lab Med., 37(4):389-95 (1999)
	.C46.	Reedy et al., "Pericellular mobilization of the tissue-destructive cysteine proteinases, cathepsins B, L, and S, by human monocyte-derived macrophages" 92 Proc. Natl. Acad. Sci. 3849-853 (1995)
	C47	Rohde et al., "Circulating cell adhesion molecules are correlated with ultrasound-based assessment of carotid atherosclerosis" 18 Arterioscler. Thromb. Vasc. Biol. 1765-70 (1998)
	C48	Rohde et al., "Plasma concentrations of interleukin-6 and abdominal aortic diameter among subjects without aortic dilatation" 19 Arterioscler. Thromb. Vasc. Biol. 1695-1699 (1999)
	C49	Ridker et al., "Prospective studies of C-reactive protein as a risk factor for cardiovascular disease" 46 J. Investig. Med. 391-395 (1998)
	C50	Schiller <i>et al.</i> , "Synthesis of side-chain to side-chain cyclized peptide analogs on solid supports" 25 Int. J. Pent. Prot. Res. 171 (1985)
	C51	Schonbeck et al., "Regulation of matrix metalloproteinase expression in human vascular smooth muscle cells by T lymphocytes" 81 Circ. Res. 448-54 (1997)
	C52	Shi et al., "Molecular cloning of human cathepsin O, a novel endoproteinase and homologue of rabbit OC2" 357 FEBS Lett. 129-34 (1995)
	C53	Shimode <i>et al.</i> , "Diagnosis of cerebral amyloid angiopathy by enzyme-linked immunosorbent assay of cystatin C in cerebrospinal fluid" 22 Stroke 860-66 (1991)
	C54	Skaleric et al., "Immunochemical quantitation of cysteine proteinase inhibitor cystatin C in inflamed human gingiva" 34 Arch. Oral. Biol. 301-305 (1989)
	C55	Snider, "Emphysema: the first two centuries-and beyond: a historical overview, with suggestions for future research: Part 2" 146 Am. Rev. Respir. Dis. 1615-622 (1992)
	C56	Stemmer et al, "Single-step assembly of a gene and entire plasmid from large numbers of oligodeoxyribonucleotides (gene synthesis; plasmid synthesis; β-lactamase; in vitro recombination; assembly PCR; DNA shuffling; mutagenesis)" 164 Gene 49-53 (1995)
	C57	Su et al., "Up-regulation of tissue inhibitor of metalloproteinases-3 gene expression by TGF-β in articular chondrocytes in mediated by serine/threonine and tyrosine kinases" 70 J. Cell. Biochem. 517-27 (1998)
	C58	Sukhova <i>et al.</i> , "Expression of the elastolytic cathepsins S and K in human atheroma and regulation of their production in smooth muscle cells" 102 J. Clin. Invest. 576-83 (1998)
	C59	Szekanecz et al., "Human atherosclerotic abdominal aortic aneurysms produce interleukin (IL)-6 and





Applicant U.S.S.N.:		The state of the s
B14 41		OTHER SON PATENT LITERATURE DOCUMENTS
Exam Initials	Cite No.	Name of Author, Title (when appropriate), Publication, Volume, Page(s), Date, Etc.
		interferon-gamma but not IL-2 and IL-4: the possible role for Il-6 and inferon-gamma in vascular inflammation" 42 Agents & Actions 159-62 (1994)
	C60	Tangirala et al., "Quantitation of atherosclerosis in murine models: correlation between lesions in the aortic origin and in the entire aorta, and differences in the extent of lesions between sexes in LDL receptor-deficient and apolipoprotein E-deficient mice" 36 J. Lipid Res. 2320-328 (1995)
	C61	Tetley, "New perspectives on basic mechanisms in lung disease 6: proteinase imbalance: its role in lung disease" 48 Thorax 560-65 (1993)
	C62	Thompson <i>et al.</i> , "Production and localization of 92-kilodalton gelatinase in abdominal aortic aneurysms" 96 J. Clin. Invest. 318-26 (1995)
	C63	van Ree <i>et al.</i> , "Increased response to cholesterol feeding in apolipoprotein C1-deficient mice" 305 Biochem J. 905-11 (1995)
	C64	Warfel <i>et al.</i> , "Constitutive secretion of cystatin C (γ-trace) by monocytes and macrophages and its downregulation after stimulation" 166 J. Exp. Med. 1912-917 (1987)
	C65	Werb et al., "Extracellular matrix remodeling during morphogenesis" 857 Ann. N.Y. Acad. Sci. 110-18 (1998)

* a copy of this reference is not provided as it was previously cited by or submitted to the office in a prior application, Serial _, and relied upon for an earlier filing date under 35 U.S.C. §120 (continuation, continuation-in-part, and divisional applications).

Examiner Signature		Date Considered	
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EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. These references are not presented with this IDS, as they were previously submitted with this application on August 2, 2001. This 1449 is solely being resubmitted in response to examiner's request for corrections.

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